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Prevalence of fungal biofilms in patients with nasal polyposis: a systematic review

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ABSTRACT

Introduction: There are many internal and external factors that are considered as the main causes of nasal infections and inflammation in chronic rhinosinusitis (CRS) leading to polyposis. It is suggested that bacterial and fungal elements have an important role in the development of these diseases.
Method: Scopus and PubMed were searched thoroughly on 1 February 2015 with the following search terms: (fungal biofilms) AND (nasal polyposis) to find the articles in which the prevalence of fungal biofilms had been evaluated in patients with nasal polyposis. Only English language articles with no time limitation were included in this study.
Result: Of 48 records found by initial search, only 10 articles met the inclusion criteria. Data showed that the presence of biofilms is associated with nasal polyposis in 110 of 303 patients and 13 of controls.
Discussion: The results of studies confirm that the fungal biofilms play an important role in the pathogenesis of chronic rhinosinusitis with nasal polyposis.
Conclusions: According to the results of included studies, there is a close association between the presence of fungal biofilm and different types of nasal disorders including nasal polyposis.

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Introduction

Chronic rhinosinusitis (CRS) with sinonasal mucosal inflammation is known to be one of the most common inflammatory diseases of the ear, nose and throat with a frequency of 16% in adults (1). This disease is responsible for a large number of hospital admissions and could adversely affect the quality of life (2,3). CRS is classified into two main groups depending on the presence or absence of nasal polyposis. Nasal polyposis is a chronic inflammatory disease of sinonasal mucosal membrane in the form of round, gelatinose, smooth, and pedunculated surface which grows in inflamed tissue of the nasal mucosa inward the nose. The prevalence of nasal polyposis is about 1% to 4 % with more frequency in adults than in children younger than 10 years of age (4).

Fungal and bacterial colonies are typically classified into two main forms including planktonic prokaryotes or eukaryotic cells as a complex, which are known as biofilms (5). Almost 99% of all bacteria are found in the form of biofilms (3). Biofilms are an accumulation of microbial or fungal cells attached to the living and non-living surfaces (6). Biofilms can be formed by a mixture of bacterial and fungal species. They are more resistant to antimicrobial agents compared to planktonic cells. Factors associated with the increased resistance include structural complexity of biofilm, the pres-

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ence of extracellular matrix and the expression of outflow pump genes associated with biofilm (5).

Although there is no single etiological factor that is responsible for the development of nasal polyps, allergies, bacterial infections, fungal infections and environmental pollutants have been suggested as the primary stimulants of the lateral nasal wall inflammation to develop nasal polyposis (4). Over the past 20 years, a range of internal and external factors associated with the onset and persistence of inflammation in CRS have been proposed. Nevertheless, microorganisms are considered as the most important external factors (1). Recently, it has been shown that bacterial and fungal biofilms could be the major contributing factors in nasal polyposis, and CRS. Moreover, biofilms are present in the sinus mucosa of patients with CRS (1). Therefore, in this literature review, we emphasize on the relationship between the prevalence of fungal biofilms and occurrence of nasal polyposis, and discuss current research in this field.

Methods

Literature search strategy

Scopus and PubMed were systematically searched to find the articles in which the prevalence of fungal biofilms had been evaluated in patients with nasal polyposis. Both databases were searched for "fungal biofilms" and "nasal polyposis" in the title, keywords, and abstracts on 1 February 2015. Relevant articles with the following search terms: (Fungal biofilms) AND (nasal polyposis) were selected and reviewed by two reviewers independently. Irrelevant articles were omitted in several step by step processes of article selection. Full texts of the relevant documents were then fully reviewed for data extraction. The reference lists of articles were also searched to include other relevant articles and to minimize the possibility of bias or any missing data.

Study selection

No time limitation was defined, but articles in languages other than English were excluded from the study to minimize any misinterpretation of data in further processes of data extraction. All types of the articles including the cross-sectional studies, clinical trials, case series, and cohort studies were included in this study. However, review articles, meta-analysis, and book chapters were excluded. Inclusion criteria of the selection of articles were documents in which the occurrence of nasal polyposis in patients correlated with the presence of fungal biofilms. Duplicated and irrelevant documents were omitted in the first step by reviewing the title and abstract of papers. Exclusion criteria were the articles in which the presence of fungal biofilm were not linked to nasal polyposis, or it was due to bacterial or histopathological infections. Moreover, studies conducted on animal models or in vitro, were excluded from further assessment.

Data synthesis

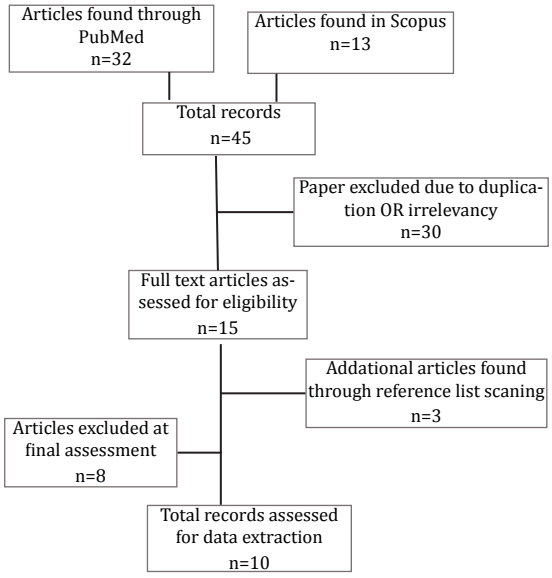
Data including the name of first author, country of origin, publication date, study design, and concluded results were extracted and tabulated. All available data including total number of participants, type of assessment, demographic data, and collected results were obtained as possible. Data were categorized based on the results reporting the association between the presence of fungal biofilms and different types of nasal disorders with most emphasis on the presence of nasal polyps. All processes of data extraction and study selection were based on the recommendation of PRISMA 2009 Checklisteach group (7).

Results

Search results

Overally, 32 articles were found in PubMed search, and 13 records were found in Scopus. Only 15 articles were seemed to be relevant in the first step to the purpose of this study. Another 3 records were also found through the reference list scanning of previously included relevant articles. After carefully reviewing of the included articles, only 10 papers met the inclusion criteria for further assessment. The rest of the articles were excluded due to publication of articles in languages other than English, studies on animals or irrelevancy. Finally, full texts of 10 articles, which met the inclusion criteria, was obtained and the data were extracted based on the main purpose of this study. Figure 1 shows step by step selection process of the articles.

Figure 1. Flowchart for selection of the studies



Description of the included studies

The total number of participants was 433 patients in the selected literatures in which the relationship between the presence of fungal biofilm and nasal polyposis had been evaluated. Among these articles, 303 were diagnosed with CRS with the presence or history of nasal polyposis, or the presence of fungal biofilm, and 130 were healthy controls or patients with nasal disorders other than rhinosinusitis. Because age and sex ratio have not been mentioned in some studies, data could not be categorized and analyzed based on demographic data. The number of studied participants varied from 1 patient in a case report to 107 patients in a retrospective study among the included studies.

Study results

Data show that the presence of biofilms is associated with nasal polyposis in 110 of 303 patients and in 13 controls. This shows that only 13 healthy controls with no sign of nasal polyps were positive for fungal biofilms. Therefore, findings indicate that the presence of fungal elements could significantly increase the risk of nasal infection and obstruction. Hence, the results of this systematic review show that there might be a strong association between the presence of fungal biofilm and CRS with nasal polyposis. Based on the results of included studies, bacterial and fungal biofilms were present together in most both cases, and patients who were positive for a single organism biofilms mostly had mild disease. Table 1 shows the extracted data in articles.

Table 1. Data extracted from included studies

Author Year , Country Reference	Study design®	Sample size	Method of detection	Findings
Gelardi 2013, Italy (8)	RS[1]	107 biofilms positive 60 controls	Light microscope with MGG[2]	32 patients (24%) with nasal polyps
Tóth 2013, Hungary (2)	CC[3]	27 CRSwNP[4] patients 6 controls	OCT[5]	5 fungal and 2 combined biofilms positive patients
Tóth 2011, Hungary (3)	PBOS[6]	50 patients with CRS/NP[7] 12 controls	Histopathological examination with HE[8]	8 fungal and 11 combined biofilms in patients
Bezerra, 2011, Brazil (9)	CS[9]	33 CRSwNP patients 27 controls	SEM[10]	24 (72.7%) of the patients and 13 (48.1%) of controls with biofilms
Tineke 2013, Saudi Arabia (10)	RS	13 CRSwNP patients, 12 control	Confocal microscopy and -FISH[11]	No fungal biofilm in patients or controls
Foreman 2009, Australia (11)	PBOS	36 biofilm positive patients, 10 controls	Confocal scanning laser microscopy	Presence of polyps in 17 patients
Foreman 2010, Australia (12)	RS	24 patients with CRS[12]	FISH	No fungal biofilms
Marianella 2013, USA (13)	CR[13]	1 woman with bilateral polyposis	Light microscopy with PAS[14]	Allergic fungal sinusitis
George 2010, USA (14)	CR	1 woman with allergic fungal sinusitis	Computed tomography	Presence of polyposis
David 2008, USA (15)	PCS[15]	11 patients with rhinosinusitis 3 controls	Epifluorescent microscopy	9 of 10 fungal positive patients had polyposis

[1]RS: retrospective study; [2]MGG: May-Grunwald Giemsa ;[3]CC: Case–control study; [4]CRSwNP: Chronic rhinosinusitis with nasal polyposis; [5]OCT: Optical coherence tomography; [6]PBOS: prospective, blinded observational study; [7]CRS/NP: chronic rhinosinusitis with nasal polyposis ; [8]HE: Hematoxylin–eosin; [9]CS: Cross-sectional study; [10]SEM: Scanning electron microscope; [11]FISH: Fluorescence in situ hybridization; [12]CRS: chronic rhinosinusitis; [13]CR: case report; [14]PAS: periodic acid- Schiff; [15]PCS: prospective controlled study

In this study, limitations included the small number of enrolled patients in studies. Furthermore, in some studies, demographic data had not been mentioned or categorized according to the purpose of the study. Therefore, in this literature review, we could not sort the data according to age and sex.

Discussion

CRS and other types of nasal disorders are poorly understood regarding pathological aspect. Recently, potential role of biofilms has been studied in different types of nasal infection, and the presence of these elements is evidently shown on the sinus mucosa of the patients with CRS.

Results of studies showed a strong association between the presence of biofilm and different types of nasal disorders including nasal polyposis, CRS, adenoid hypertrophy, and other nasal infections. Moreover, it was shown that the presence of biofilms significantly associates with the degree of nasal obstruction (8). Some studies demonstrated synergism between bacteria and fungi in most patients with CRS and nasal polyposis (1). Despite the role of bacteria in the pathogenesis of CRS and other nasal infections, it has been shown that fungi can also have an important role in the pathogenesis of nasal polyposis. On the other hand, although microbial biofilms are more prevalent than fungal biofilms in CRS and nasal polyposis, studies showed that bacterial biofilms might also be present in healthy controls with less fungal biofilms in this population (11). Therefore, it can be concluded that fungal biofilm might represent the presence of nasal polyposis. Furthermore, fungal biofilms are the most important health problem associated with significant rates of mortality. Aspergillus fumigatus, as the most prevalent fungal species, has been associated with different types of infections (16). As well, in the present review, Aspergillus was the most important fungal species associated with nasal polyposis.

Conclusion

Based on the data obtained from included articles, a close relationship could be found between the presence of fungal biofilms and chronic rhinosinusitis with nasal polyposis (CRS/NP). Moreover, it could be assumed that the presence of fungal biofilms might serve as a prognostic factor of further fungal infections of the nose, and might be of great help in finding the drug of choice for the treatment of infections.

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Conflict of Interest

The authors declare no conflict of interest.

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